MODELLING AND ANALYSIS OF BILE FLOW IN HUMAN BILIARY SYSTEM

A Syonpsis submitted for

The partial fulfillment of Degree of

Doctor of Philosophy

In

Mathematics

Submitted by
TANUJ KUMAR RAWAT

Prof. S. P. Singh
Supervisor

Prof. Ravinder Kumar
Head

Department of Mathematics
Faculty of Science
Dayalbagh Educational Institute
(Deemed University)
Dayalbagh, Agra-282005
2019

TABLE OF CONTENTS

1. Introduction ……..….1-2

2. Related Preliminaries ……...……...3-11

2.1. Human Biliary System……...3-4

2.2. Functions of the biliary system……...…….4

2.3. Composition of bile……...…….…..6-7

2.4. Function of Gallbladder……...…….7

2.5. Gallstones……...……..7-8

2.6. Fluid……...……..8

2.7. Viscosity……...……....8-9

2.8. Newtonian and Non-Newtonian Fluid……..…..……9-10

2.9. Carreau's fluid equation……..…..….....10-11

3. Survey of Literature ……..11-16

4. Purpose of study……...…16

5. Proposed work…….……..17-19

6. Methodology……...…19

7. Motivation…….……..20

8. Expected outcomes…….……20

References……..…21-25

1. Introduction

The main functions of the human biliary system are the producing, storage, and bile transport into the duodenum, (Fig. 1) (liver, gallbladder, biliary tree /hepatic ducts, cystic duct, common bile duct, major duodenal papilla).The bile plays a role in the fat emulsification and digestion regulation. The bile flow dynamics depends on the efficiency of the gallbladder, which plays a significant role in the physiology of the biliary system. Some factors, such as pregnancy, taking certain drugs (affecting cholesterol and bilirubin metabolism), obesity, fasting, eating fatty foods, metabolic disorders, diabetes mellitus, etc. lead to changes in the chemical composition of bile, which acquires the ability to form gallstones. Another reason of the gallstones formation is the improper gallbladder performance during refilling and emptying stages. It is known that long-term bile stasis may lead to gallstones and some serious diseases such as cholecystitis, pancreatitis, jaundice and others.

Recently, there was an association between presence of gallstones and biliary pain [29]. There was reported an increase of the gallbladder disease by 18.3% from 2005 to 2015 years.

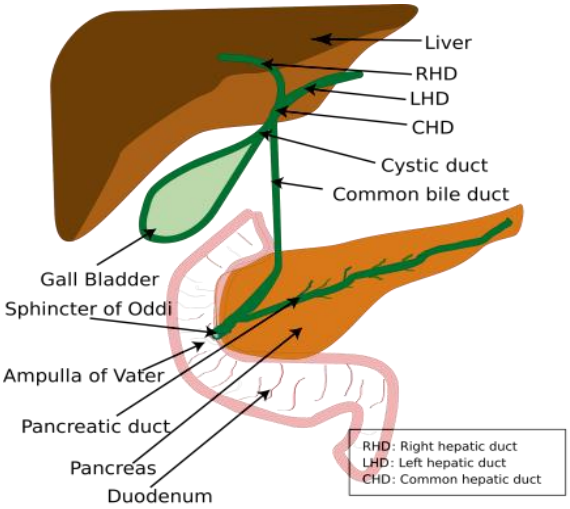

Fig.1. Biliary system [28]

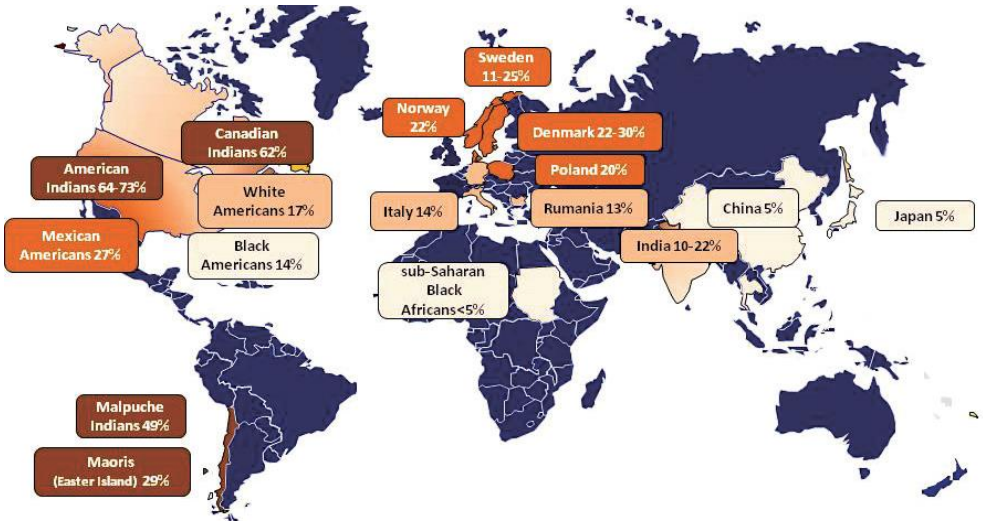

Fig.2. worldwide prevalence of gallstones/biliary pains based on ultra-sonographic surveys [29]

Geography and ethnicity, in particular, plays an enormous role in the prevalence of gallstone disease and the type of stone that forms. Cholesterol gallstones predominate in the developed countries of the Western world while brown pigment stones in the bile ducts are more common in Asia (Fig. 2).

In India, the prevalence of cholelithiasis was 10-22%, depending on sex, which is one of the highest rates in the world. In Russia, along with the countries of Northern Europe, where the incidence rate varies at a level of 15% of the population, about 20 million people suffer from cholelithiasis. Indicators of India in the disease of cholelithiasis have grown in recent years, which indicate the relevance of research in the country.

Cholecystectomy (surgical gallbladder removal) is the most commonly performed abdominal operation in the West. This operation is usually adopted for the treatment of the patients suffering from the gallbladder disease and biliary pain.

2. Related Preliminaries

2.1 Human Biliary System

The human biliary system consists of the organs and ducts i.e. common bile duct, cystic duct, left hepatic duct, right hepatic duct and common hepatic duct, which are involved in the production and transportation of bile. The transport of bile from the liver hepatocyte (bile is produced in hepatocyte) to the small intestine is accomplished via a system of bile ducts that collectively are called the biliary system.

The biliary system consists of canaliculi, i.e. spaces between adjacent hepatocyte cells. Further towards the small intestine each canaliculus feeds into a true bile duct. Small bile ducts join together to form a large and common bile duct, which dumps bile into the duodenum (a part of the small intestine). A powerful muscle known as a sphincter is located at the entry point to the small intestine, and its functions to control the flow rate of the bile [28].

The anatomy of the human biliary system consists of-

I. The Liver

II. The Gallbladder

III. The Biliary Tract

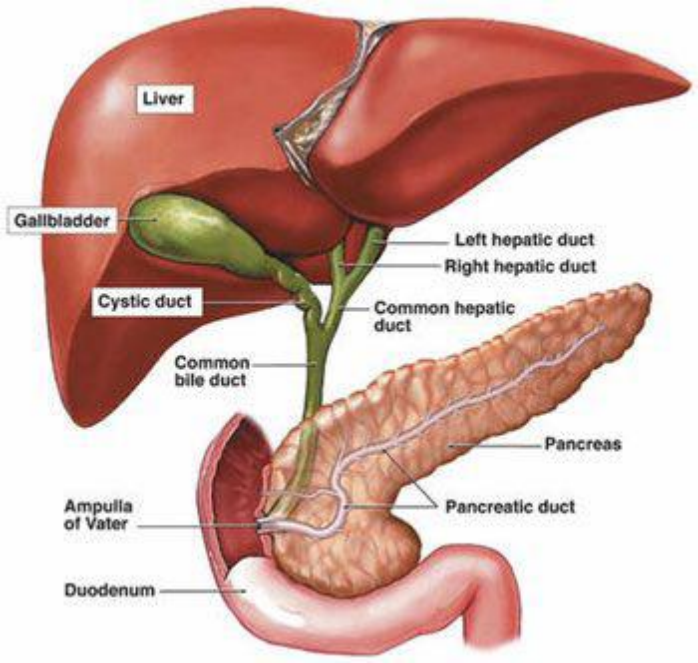

Fig.3. Human Biliary System [28]

2.2. Functions of the biliary system

The main function of biliary system includes the following:

- to drain waste products from the liver into the duodenum
- to help in digestion with the controlled release of bile.

Liver

The liver is a vital organ present in vertebrates and other animals. This organ plays a vital role in metabolism and has a number of functions including glycogen storage, decomposition of red blood cells, hormone production and detoxification. It produces bile, an alkaline compound which helps in the digestion of lipids.

Gallbladder

The gallbladder is a pear-shaped organ that stores and concentrates bile. It is approximately 3 inches to 4 inches long and about 1 inch wide. The gallbladder stores about 50 ml of bile, which is released when

food containing fat enters the digestive tract. The bile emulsifies fats in partly digestive food. Food stimulates the production of a hormone called cholecystokinen, which acts to trigger the secretion of bile.

Biliary Tract

The biliary tract (or biliary tree) is the common term for the path by which bile is secreted by the liver on its way to the duodenum. It is referred to as a tree because it begins with many small branches which end in the common bile duct. Pressure inside the biliary tree can give rise to gallstones.

Mechanism of bile flow in biliary tract

1. When the liver cells secrete bile, it is collected by a system of ducts that flow from the liver through the right and left hepatic ducts. These ducts ultimately drain into the common hepatic duct.

2. The common hepatic duct then joins with the cystic duct from the gallbladder to form the common bile duct, which runs from the liver to the duodenum.

3. When food is eaten, the gallbladder contracts and releases stored bile into the duodenum to help break down the fats

The biliary tract comprises of the following three ducts:

- Cystic duct
- Common hepatic duct
- Common bile duct

Cystic Duct

The cystic duct is the short duct that joins the gallbladder to the common bile duct. The presence of the "Valves of heister" in the lumen complicates the cystic duct geometry. These valves consist of several semi lunar folds. The number of folds in the cystic duct varies from 2 to 14. The diameter of cystic duct ranges from 2mm to 5 mm and its length is 60 mm. The system of human cystic duct functions as a single conduit for the transport of bile during both filling and emptying of the gall bladder.

Common Hepatic Duct

The common hepatic duct is the duct formed by the convergence of the right hepatic duct and the left hepatic duct. The common hepatic duct joins the cystic duct to the common bile duct.

Common Bile Duct

This duct carries bile from liver and the gallbladder into the duodenum (the upper part of the intestine).

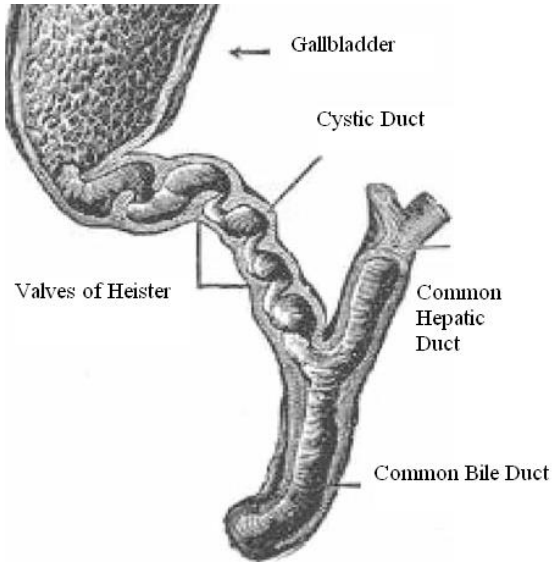

Fig.4**.** The Anatomy of the human biliary tract showing part of the Gallbladder neck connected to the spiral valves in the cystic duct.

2.3. Composition of bile

Bile is a bitter-tasting, dark green to yellowish brown fluid, produced by the liver that aids the process of digestion of lipids in the small intestine. Bile is stored in the gallbladder and on eating, it is discharged into the duodenum. Bile is a composition of the following materials: water, bile salts, bilirubin and cholesterol. It is produced in hepatocyte, which are the main functional cells of the liver and flows into the bile ducts. It is modified by the addition of secretions from the epithelial cells. The main route for eliminating cholesterol from the body is through the bile. Cholesterol, being fatty in composition, cannot dissolve in the water-based fluids that are present in the body. Bile salt is the actual component which helps in the breakdown and absorption of fats. The bile acids and lecithin in bile allow cholesterol to dissolve into solution. If this mechanism goes wrong, cholesterol can precipitate out of the bile solution, forming gallstones. Aside from its function as waste disposal fluid, bile also helps neutralize stomach acid in the small intestine, providing a more hospitable environment for enzymes that break down food.

Function of bile acids to promote the complete digestion of food, by facilitating the uptake of fat-soluble vitamins through the wall of the small intestine [28].

2.4 Function of Gallbladder

The function of the gallbladder is to store and concentrates bile. The bile emulsifies fats and neutralizes acids in partly digested food.

Conditions and Diseases of gallbladder

Sometimes the substances contained in bile (like cholesterol) crystallizes in the gallbladder leading to the formation of stones called gallstones. They can cause inflammation of gallbladder. Most common biliary diseases are:

- Cholelithiasis - the presence of gallstones and
- Cholecystitis – the inflammation of gallbladder

2.5 Gallstones

Gallstones are small, pebble-like substances that develop in the gallbladder. Gallstones form when liquid stored in the gallbladder hardens into pieces of stone-like material and if the liquid bile contains too much cholesterol, bile salts, or bilirubin, it can harden into two types of gallstones cholesterol stones and pigment stones.

Sometimes gallstones passing through the common bile duct provoke inflammation in the pancreas called gallstone pancreatitis which is extremely painful and potentially dangerous condition. If any of the bile ducts remain blocked for a significant period of time, severe damage or infection can occur in the gallbladder, liver, or pancreas. If left untreated, the condition can be fatal.

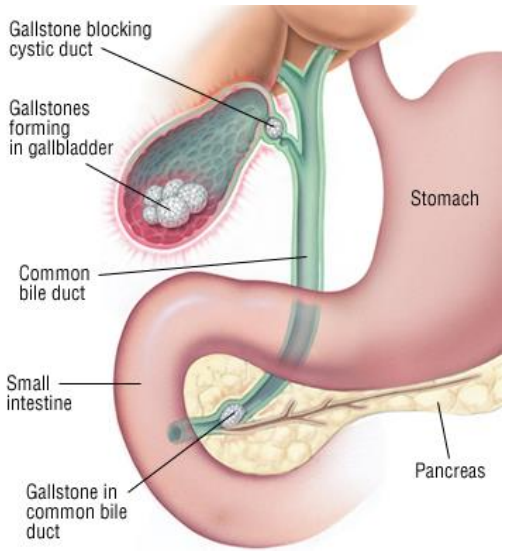

Fig.5. Biliary System with gallstone

2.6 Fluid

The defining property of the fluid lies in the ease with which they can be deformed. The fluid consists of liquids and gases. The most important difference between them is there compressibility [10]. Gases can be compressed much more easily. Fluids are assumed to obey the continuous assumption. Fluids are composed of molecules that collide with one another and solid objects. However, the continuum assumption considers fluids to be continuous, rather than discrete. Consequently, properties such as density, pressure, temperature, and velocity are taken to be well-defined at infinitesimally small points, and are assumed to vary continuously from one point to another [10].

2.7 Viscosity

Viscosity is a measure of the resistance of a fluid which is being deformed by either shear or tensile stress. In everyday terms (and for fluids only), viscosity is "thickness" or "internal friction". Thus, water is "thin", having a lower viscosity, while honey is "thick", having a higher viscosity. The less viscous the fluid is, the greater its ease of movement (fluidity). Viscosity describes a fluid's internal resistance to flow and may be thought of as a measure of fluid friction. With the exception of superfluids, all real fluids

have some resistance to stress and therefore are viscous, but a fluid which has no resistance to shear stress is known as an ideal fluid or Inviscid fluid. It can be said that: Internal friction (viscosity) implies-

- Viscous fluid: there is internal friction
- Non-viscous fluid: internal friction is negligible
- Ideal fluid: incompressible and non-viscous [28]

Viscosity coefficients

Viscosity coefficients can be defined in two ways:

- Dynamic viscosity, also absolute viscosity (units Pa·s, Poise).
- Kinematic viscosity is the dynamic viscosity divided by the density (units cm^2/s, Stokes).

2.8 Newtonian and Non-Newtonian Fluid

Newtonian fluids which obey Newton's Law of viscosity which says that shear stress is directly proportional to shear rate. Example: Water, air, mercury.

The constitutive equation for Newtonian fluids is:

$$\tau = \mu e$$

Where τ is shear stress, e is shear rate. The ratio of shear stress and the shear rate is constant which is termed as coefficient of viscosity denoted by **μ [10].**

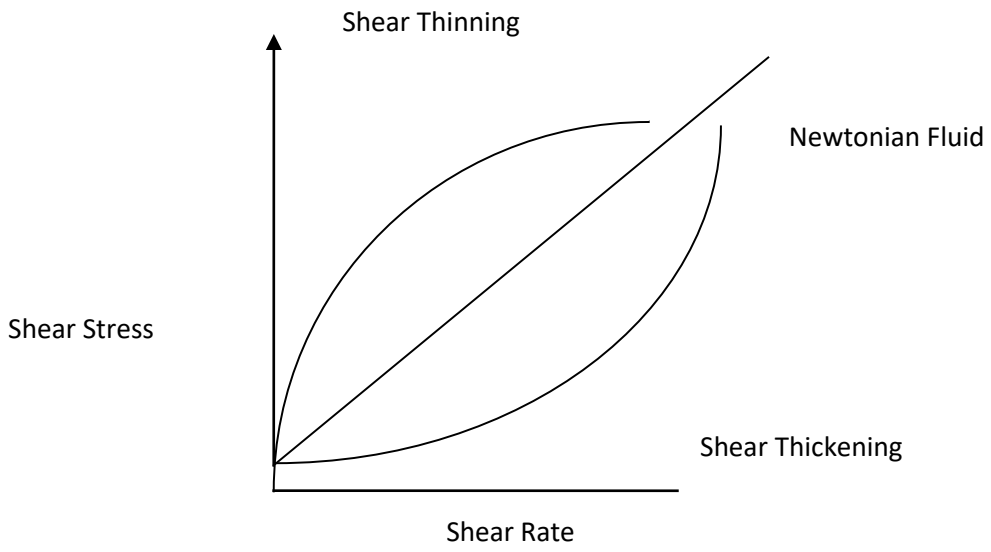

Fig.6. graph between shear stress shear rate [10]

Non-Newtonian Fluids are those fluids which do not obey Newton's law of viscosity. For these, ratio of shear stress to shear rate is non-constant. Example: paints, jam, polymer solution [10].

2.9 Carreau's fluid equation

The constitutive relation for the non-Newtonian fluid flow describe Carreau's equation [12]

$$\overline{S_{ij}} = -p\delta_{ij} + \overline{\tau_{ij}}$$

$$\overline{\tau_{ij}} = \left[\eta_\infty + (\eta_0 - \eta_\infty)(1 + ((\Gamma\bar{\dot{\gamma}})^2)^{\frac{m-1}{2}})\right]\bar{\dot{\gamma}}_{ij}$$

Where p is the pressure, δ_{ij} is kronecker delta, τ_{ij} is the extra stress tensor, η_0 is the zeo shear rate viscosity, η_∞ is the infinite shear rate, Γ is the time constant , m is the power index . The shear rate $\bar{\dot{\gamma}}$ is defined as follows:

$$\bar{\dot{\gamma}} = \sqrt{\frac{1}{2}\sum\sum \bar{\dot{\gamma}}_{ij}\bar{\dot{\gamma}}_{ji}} = \sqrt{\frac{1}{2}\Pi}$$

Where π is the second invariant strain rate tensor. In case of η_∞ and applying Taylor's expansion on $\bar{\tau}_{ij}$, equation takes the form:

$$\bar{\tau}_{ij} = \left[\eta_{ij} + \frac{m-1}{2}((\dot{\gamma})^2)\right]\bar{\dot{\gamma}}_{ij}$$

3. Survey of Literature

Master and Elman (1926) observed that after feeding a dog, a forceful contractions of the gallbladder occurred. The pressure within the gallbladder of a healthy unanesthetized dog fasted 24 to 28 hours is usually about equal to a column of bile 100 mm high. After a few swallows of food there is a rapid increase in the pressure to more than 200 mm, with a gradual fall in it again, and repeated similar rises and falls occurred thereafter. The gallbladder contractions responsible for these alterations were accompanied by a lessening in the resistance to the passage of bile to the intestine, a resistance which is maintained by the muscles at the lower end of the common duct. There would appear to be a reciprocal response on the part of the two structures to the one stimulus [20].

Holzbach et al. (1973) described a direct method for measuring the maximum cholesterol solubility in bile. Application of this method to five large mammalian species, including man produced a micellar zone significantly smaller than that already reported. Further, studies on invitro model solution patterned after bile confirmed this new micellar zone. Thus, direct evidence demonstrated that the micellar zone boundary derived invitro from model solutions was applicable to human gallbladder bile. Using the present criteria, normal human bile, in contrast to bile from other mammalian species, is commonly supersaturated with cholesterol. A male–female difference in bile composition is not demonstrable despite the well–established female preponderance of cholelithiasis. Bile from patients with cholesterol cholelithiasis has a micellar zone similar to normal but differs compositionally in that there is a greater excess of cholesterol above saturation .Thus, they concluded that cholesterol super saturation may be a necessary but not solely sufficient cause for gallstones formation [7].

Rodkiewicz et al. (1978) conducted experiments showing that bile flowing in a rigid tube, behaves like a Newtonian fluid. The immediate result of this development was that the analytical and experimental finding available from fluid mechanics and heat transfer principle which are applicable to the laminar flow of Newtonian fluid, may be used to understand the flow phenomena of bile in the human biliary tree, in both qualitative and quantitative manner [26]. He (1979) also developed a mathematical model of the mechanical factors affecting the flow of bile. It was found that the rate of flow of bile in a duct of extrahepatic biliary tree is related to the associated pressure drop by using the power law fluid model [27]. Pitt et al. (1982) observed that cystic duct resistance increases while sphincter of oddi resistance is unchanged in the presence of lithogenic bile without gallstones. They tested the hypothesis before gallstone formation, stasis results from increased cystic duct resistance and altered gallbladder compliance. Thus, cystic duct resistance increased but gallbladder compliance was unchanged before gallstone formation [25].

Norman et al. (1984) proposed a simple mathematical model to account for the coupling of secretion rates of bile salts, lecithin and cholesterol into bile. The model presented by them, described the quantitative relationship between BS (Bile Salts), L (Lecithin) and Ch (Cholesterol) secretion into bile and had applied this model to analyse a wide range of physiological and biochemical data from man and other species [21].

Jungst et al. (1993) suggested that the super saturation and rapid nucleation of cholesterol in bile were of key importance in the pathogenesis of cholesterol gallstones. The effects of bile acids and phospholipids on cholesterol saturation of bile had been extensively studied; their influence on the cholesterol nucleation time has not been compared. Therefore, investigation was done to find whether increases of bile acid or phospholipid concentration in bile by invitro supplementation affect the cholesterol nucleation time. The increase of phosphatidycholine or bile acid concentration decreased the mean cholesterol saturation index to a similar extent. Supplementations of bile with increasing amount of synthetic or biliary PCs(Post cholecystectomy syndrome) caused a marked prolongation of the nucleation time in bile. It was

speculated that increasing phospholipid concentrations in bile might be more effective for the prevention of cholesterol gallstones than increasing bile acid concentrations [8]. Further they (2001) also found that the viscosity of gallbladder bile is markedly higher than that of hepatic bile in patients with gallstones. The concentration of mucin was the major determinant of biliary viscosity and may contribute by this mechanism to the role of mucin in the pathogenesis of gallstones [9].

Li et al. (2002) developed a mechanical model for the human biliary system during the emptying phase, based on a clinical test in which gallbladder volume changes were measured in response to a standard stimulus and a recorded pain profile. The model described the bile emptying behavior, the flow resistance in the biliary ducts, the peak total stress, including the passive and active stresses experienced by the gallbladder during the emptying [15]. They also (2007) worked on one dimensional model to estimate the pressure drop in the normal human biliary system for Reynolds number up to 20. Excessive pressure drop during bile emptying and refilling may result in incomplete bile emptying, leading to bile stasis and subsequent gallstones formation. The effects of biliary system geometry, elastic property of cystic duct and bile viscosity on pressure drop was studied. It was found that the maximum pressure drop occurs during bile emptying immediately after a meal, and was greatly influenced by the viscosity of bile and the geometric configuration of the cystic duct (i.e.) the patients with more viscous bile or with a cystic duct containing more baffles or a larger length had the greatest pressure drop. It was found that the most significant parameter was the diameter of the cystic duct [16]. In (2008) they extended their previous study of the human biliary system to include two new factors: the non–Newtonian properties of bile, and elastic deformation of the cystic duct. A one – dimensional (1D) model was analyzed and compared with three–dimensional fluid structure interaction simulations. It was found that non – Newtonian bile raises resistance to the flow of bile, which can be increased enormously by the elastic deformation (collapse) of the cystic duct [17].

Duch et al. (2002) quantified the structural and mechanical changes in the CBD (common bile duct) at different time intervals after acute obstruction. Biliary obstruction in man, most often caused by cholelithiasis, induced remodeling of the bile ducts. The collagen area increased during obstruction but no

correlation between the size of the collagen area and biomechanical parameters was found. A practical implication of the present study serves as a warning to surgeons. It was suggested that operative procedures such as suturing, anastomosis and procedures must be performed with special care to avoid damage to the CBD [6].

Ooi et al. (2003) discussed the simulation of the biliary system, that includes deformable feature of the cystic duct and investigate its role in cystic duct resistance using fluid–structure interaction technique [23]. They (2004) also presented a numerical study of steady flow in human cystic duct models. Idealized models were constructed, first with staggered baffles in a channel to represent the valves of Heister and lumen. Numerical simulations of bile flow in cystic duct models was conducted to investigate the function of cystic duct in gallstone formation. It was found that the most vital geometric factor responsible for increasing cystic duct resistance is the baffle clearance, followed by the number of baffles, while the least important are the angle between the duct and gallbladder. It was hypothesized that patients with a small lumen and large number of valves of Heister are more likely to develop gallstones, since the higher resistance through the duct will promote stasis of bile in the gallbladder [24].

Dang et al. (2004) presented the structural and mechanical re-modeling of the common bile duct. The net effect of the structural and mechanical remodeling was to restore the stress and strain to their homeostatic values. Furthermore, the strain recovered more rapidly and more completely than stress. Finally, the remodeling data were expressed mathematically in terms of indicial response functions (IRF), i.e. change of particular feature of a common bile duct (CBD) in response to a unit step change of the pressure [5].

Al-Atabi et al. (2006) worked on cystic duct visual-based evaluation of gallstones formation risk factors. Gallstones are commonly related to the super-saturation of bile with cholesterol in the presence of nucleating agents. Clinical evidence showed that gallstones were frequent in healthy persons with complex cystic ducts geometry, an indication that fluid mechanics of the bile flow may play a role in the formation of gallstones. In order to evaluate this role, correlations between idealized cystic duct geometry and the pressure drop across had been determined both experimentally and numerically simulated with computational fluid dynamics (CFD) techniques and studied the influence of its various anatomical

structures on the resistance to bile flow [1]. In (2006) they also presented a mathematical model accounting for the effects of geometry of the baffle configurations .It predicted the pressure drop in circular pipe fitted with segmental baffles. The model was solved algebraically for flow in pipe with three baffle arrangements and the results were validated by experimental data [2]. They also studied in (2008) the role of the valves of Heister during both the filling and the emptying phases of the gallbladder. The result suggested that the existence of these valves helps both the filling and the emptying of the gallbladder by providing structural support and preventing the duct from total collapse [3].

Bird et al. (2006) described the variation in geometry of the cystic duct, obtained from acrylic resin casts of the neck and first part of the cystic duct in gallbladders removed for gallstones disease and obtained from patients undergoing partial hepatectomy for metastatic disease. The data obtained allowed the formation of number of standard terms for describing cystic duct morphology and demonstrates that the term 'spiral valve' is only partially correct when describing the duct anatomy. Also, the term valve implies active resistance to flow in one direction, whereas the internal baffles of the cystic duct would serve to regulate bile flow in both directions [4].

Luo et al. (2007) researched to understand the physiological and pathological functions of the biliary system. It was believed that the mechanical factors play an important role in the mechanism of the gallstone formation and biliary diseases. In this paper, the state of art knowledge of the fluid dynamics of bile flow in the biliary tract, the solid mechanics of the gall bladder and bile ducts, recent mathematical and numerical modeling of the system, and finally the future challenges were discussed. Moreover, the paper has reviewed the current progress in understanding the mechanical aspects of the biliary system, and covered the areas in bile fluid dynamics, bile rheology, gallbladder and duct tissue mechanics, mathematical and numerical modeling, and the correlation between the mechanical stresses and the gallbladder [18].

Maiti et al. (2011) described relevance to flow of bile within ducts in a pathological state, theoretical study of a fluid in a channel. The velocity profile and the critical pressure for the occurrence of reflux are investigated with particular emphasis by using appropriate numerical methods. The results are discussed,

in presence of gallstones, bile velocity increases as the value of the porosity parameter increases, while the critical pressure for reflux decreases as porosity increases [19].

Kuchumov et al. (2014) presents an experimental study of pathological human bile taken from the gallbladder and bile ducts. Results on the hysteretic bile behavior at loading uploading test are presented, which prove that the pathological bile is a non-Newtonian thixotropic liquid. The viscosity of the gallbladder bile was shown to be higher compared to the duct bile. It was found that at higher shear stress the pathological bile behave like Newtonian fluid, which is explained by reorientation of structural components[11]. Kuchumov et al. (2015) further study the modelling of peristaltic bile flow in the papilla ampoule with stone and its solution is devoted to the peristaltic flow of bile as Carreau's fluid. He obtained the analytical solution for axial velocity, flow rate, and pressure [12]. They (2016) also explained peristaltic flow of lithogenic bile in the vateri's papilla as non-Newtonian fluid in the finite-length tube and plotted pressure distribution versus axial coordinate at different time of instants for various values of Weissenberg number and amplitude ratio. It revealed that the amplitude ratio has more effect on the pressure distribution along the tube compared to the Weissenberg number [13]. Further they described in (2018) that fluid motion in the elastic and compliant ducts. Bile flow in the major duodenal papilla is considered as peristaltic fluid motion biliary system geometry was obtained using MRI(magnetic resonance imaging) patient-specific data. It was confirmed that normal bile can be modeled as Newtonian fluid and lithogenic bile can be non-Newtonian fluid. It will help surgeons to decrease the number of complications in population and will shorten the recovery time after surgery [14].

4. Purpose of Study

In the world, not so many scientific groups are working on the development of biomechanical models of bile flow.

This research is devoted to the study of the behavior of bile flow in the biliary system. The proposed mathematical work can be used as an element of the decision support system in surgery in the treatment of biliary disease.

5. Proposed Work

In view of various above problems, some of the following types of problems are proposed to be done:

- **Study of effect of heat transfer on bile flow in a duct.**

The governing equations of the flow in the wave frame of reference are

The equations of motion in two dimensional with heat transfer:

$$\rho\left(\frac{\partial}{\partial t}+\bar{W}\frac{\partial}{\partial \bar{X}}+\bar{U}\frac{\partial}{\partial \bar{Y}}\right)\bar{W}=-\frac{\partial \bar{p}}{\partial \bar{X}}+\frac{\partial}{\partial \bar{X}}\bar{\tau}_{xx}+\frac{\partial}{\partial \bar{Y}}\bar{\tau}_{xy}-\rho Gr\beta(T-T_0)$$

$$\rho\left(\frac{\partial}{\partial t}+\bar{W}\frac{\partial}{\partial \bar{X}}+\bar{U}\frac{\partial}{\partial \bar{Y}}\right)\bar{U}=-\frac{\partial \bar{p}}{\partial \bar{y}}+\frac{\partial}{\partial \bar{X}}\bar{\tau}_{xy}+\frac{\partial}{\partial \bar{Y}}\bar{\tau}_{yy}$$

And the equation of continuity:

$$\frac{\partial \bar{W}}{\partial \bar{X}}+\frac{\partial \bar{U}}{\partial \bar{Y}}=0$$

Where ρ is the density, $\bar{W}\ and\ \bar{U}$ are the velocity components, $\bar{p}$ is the pressure, τ_{ij} is the tensor stress, T is the temperature, β is the source sink parameter and Gr is the Grashof number.

- **Modelling of the pathological bile flow in the duct.**

The governing equations of motion and continuity in two dimensional are:

$$\rho\left(\frac{\partial u}{\partial t}+u\frac{\partial u}{\partial x}+v\frac{\partial u}{\partial y}\right)=-\frac{\partial p}{\partial x}+\mu_1\left(\frac{\partial^2 u}{\partial x^2}+\frac{\partial^2 u}{\partial y^2}\right)$$

$$\rho\left(\frac{\partial v}{\partial t}+u\frac{\partial v}{\partial x}+v\frac{\partial v}{\partial y}\right)=-\frac{\partial p}{\partial y}+\mu_1\left(\frac{\partial^2 v}{\partial x^2}+\frac{\partial^2 v}{\partial y^2}\right)$$

$$\frac{\partial u}{\partial x}+\frac{\partial v}{\partial y}=0$$

Where ρ is the density, $u\ and\ v$ are the velocity components, p is the pressure and $\mu_1 = \frac{\mu}{e}$ where μ is viscosity and e is the porosity.

- **Study of peristaltic lithogenic bile flow of a fluid in a porous channel**.

The equations of motion in two dimensional system are:

$$\rho\left(\frac{\partial}{\partial t} + w\frac{\partial}{\partial r} + u\frac{\partial}{\partial z}\right)w = -\frac{\partial p}{\partial r} + \frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial w}{\partial r}\right) + \frac{\partial^2 w}{\partial z^2} - \frac{\mu}{k_0}w$$

$$\rho\left(\frac{\partial}{\partial t} + w\frac{\partial}{\partial r} + u\frac{\partial}{\partial z}\right)u = -\frac{\partial p}{\partial z} + \frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial u}{\partial r}\right) + \frac{\partial^2 u}{\partial z^2} - \frac{\mu}{k_0}(u + c)$$

And the equation of continuity is:

$$\frac{\partial w}{\partial r} + \frac{w}{r} + \frac{\partial u}{\partial z} = 0$$

Where ρ is the density, $w\ and\ u$ are the velocity components, p is the pressure, μ is the fluid viscosity, c is the velocity of wave frame, k_0 is the permeability parameter.

- **Study of effect of wall slip condition with variable viscosity on the peristaltic bile flow.**
- **Study of effect on bile flow due to axially/radially varying viscosity in cystic duct.**

The equations motion in two dimensional system are:

$$\rho\left(\frac{\partial u}{\partial t} + u\frac{\partial u}{\partial r} + w\frac{\partial u}{\partial z}\right) = -\frac{\partial p}{\partial r} + \frac{\partial}{\partial r}\left(2\mu(r)\frac{\partial u}{\partial r}\right) + \frac{2\mu(r)}{r}\left(\frac{\partial u}{\partial r} - \frac{u}{r}\right) + \frac{\partial}{\partial z}\left[\mu(r)\left(\frac{\partial u}{\partial z} + \frac{\partial w}{\partial r}\right)\right]$$

$$\rho\left(\frac{\partial w}{\partial t} + u\frac{\partial w}{\partial r} + w\frac{\partial w}{\partial z}\right) = -\frac{\partial p}{\partial z} + \frac{\partial}{\partial z}\left(2\mu(r)\frac{\partial w}{\partial z}\right) + \frac{1}{r}\frac{\partial}{\partial r}\left[r\mu(r)\left(\frac{\partial u}{\partial z} + \frac{\partial w}{\partial r}\right)\right]$$

And the equation of continuity:

$$\frac{\partial u}{\partial r} + \frac{u}{r} + \frac{\partial w}{\partial z} = 0$$

Where ρ is the density, $u\ and\ w$ are the velocity components, p is the pressure and $\mu(r)$ is the varying viscosity.

- **Modelling of bile flow in elastic duct.**

The governing equations for the steady, laminar flow of the bile are

$$\frac{\partial u_i}{\partial x_j} = 0,$$

$$\rho u_j \frac{\partial u_i}{\partial x_j} = -\frac{\partial p}{\partial x_j} + \frac{\partial \tau_{ij}}{\partial x_j},$$

The consecutive equation for the elastic duct wall is chosen to be the 'tube law' for homogeneous elastic material:

$$p - p_c = \frac{Eh^3}{3(1-k^2)d^2}\left(\alpha^k - \alpha^{-1}\right)$$

Where u_i is bile velocity, ρ is the bile density, h is the wall thickness, k is Poisson's ratio of the elastic wall, E is the Young's modulus, τ_{ij} is the shear stress in flow field and p is the pressure.

6. Methodology

In the research work to be done, we will investigate the behavior of the pathological bile using a non-Newtonian fluid. The constitutive equations will be solved numerically and analytically using the initial conditions and the given boundary conditions to get expressions and will be analyzed graphically.

7. Motivation

Creation of patient-specific biomechanical model of bile flow at the healthy state and the pathology to evaluate an efficiency of contemporary treatment methods of the biliary disease and its complications in order to improve the patient's quality of life

8. Expected outcomes

In the study to be done, the variation of different flow parameters such as axial velocity, pressure gradient, stream function, resistance to flow will be analyzed. It is expected that the models will generate information about the impact of the stenosis, papillary stenosis, gallstone on the resistance to flow, pressure gradient, stream function and flow rate etc.

References

1. Al-Atabi, M.A., chin, S. B. and Lau, X. Y., "Cystic duct visual based evaluation of gallstone formation risk factors" , Journals of engineering science and technology, Vol. 1, No. 1, 2006.
2. Al-Atabi, M.A., chin, S. B. and Lau, X. Y., "Pressure drop in laminar and turbulent flows in circular pipe with baffles – An experimental and analytical study " ,International journals of fluid mechanics research, Vol. 33. No. 4, 2006.
3. Al-Atabi, M.A., chin, S. B. and Lau, X. Y. and Back, S., "investigation of the flow in a complaint idealized human cystic duct ", Journal of biomechanical science and engineering Vol. 3, No.3, 2008.
4. Bird, N.C., Ooi, R., Chin, S.B. and Johnson, A., "Investigation of the functional three dimensional anatomy of the human cystic duct: A single helix ", Clinical anatomy 19; 528-534, 2006.
5. Dang, Q., Gregerson, H., Duch, B. and Kasab, G.S., "Indicial response functions of growth and remodeling of common bile duct post obstruction", Am J Physiol Gastrointest Liver Physiol 286:G420-G427,2004.
6. Duch B.U., Anderson, H.L., Smith. T. and Gregarson, H., "structural and mechanical remodeling of the common bile after obstruction", Neurogastroenterology and motility Vol. 14 Issue 2, pages 111-122, 2002.
7. Holzbach, B. T., Narsh, M., Olszewski, M. and Keith, H., "Cholesterol solubility in bile Evidence that the supersaturated bile if frequent in healthy man", J Clinical Investigation, 1973 June; 52(6):1467-1479.
8. Jungst, D., Lang, T., Huber, P., Lang, V. and paumgarther, G., "Effect of phospholipids and bile acids on cholesterol nucleation time and vesicular/micellar cholesterol in gallbladder bile of patients with cholesterol stones", Journal of lipid research Vol.34, 1993.

9. Jungst, D., Niemeyer, A., Muller, L. and Pozo, R. D., “Mucin and phospholipids determine viscosity of gallbladder bile in patients with gallstones”,World J Gastroenterology, 7(2); 203-207, 2001.
10. Kapur J.N, Mathematical Models in Biology and Medicine, Affiliated East-West Press Private Limited, 1992.
11. Kuchumov A. G., Gilev V., Popov V., “Non-Newtonian flow of pathological bile in the biliary system: experimental investigation and CFD simulation”, Korea-Australia Rheology Journal, Vol.26, No.1, pp.81-90 feb 2014.
12. Kuchumov A. G., “Modelling of peristaltic bile flow in the ampoule with stone and in the papillary stenosis cases: application to reflux investigation”, researchgate.net, Vol. 52, 2015.
13. Kuchumov A. G., “Mathematical modelling of the peristaltic lithogenic bile flow through the duct at papillary stenosis as a tapered finite-length tube”,Vol. 20, No. 2: 77-96 ,Russian journal of biomechanics, 2016.
14. Kuchumov A. G., “Biomechanical modelling of bile flow in the biliary system”, MATEC Web of conference 145, 04004, 2018.
15. Li, W. G., Luo, X. Y., Bird, N. and Johnson, A., “Correlation of mechanical factors and gallbladder pain”, J of computational and mathematical methods in medicine.
16. Li, W., Chin, S.B., Johnson, A. and Bird, N. C., “One dimensional models of the human biliary system”, Vol. 129, 2007.
17. Li, W. G., Luo, X. Y., Chin, S.B., Hill, N. A., Bird, N. C., and Johnson, A., “Non-Newtonian bile flow in elastic cystic duct: one and three dimensional modeling”, Annals of Biomedical Engineering, Vol.36, No.11,2008.
18. Luo, X. Y., Li, W., Bird, N., Chin, S. B. and Johnson, A., “On the mechanical behavior of the human biliary system”, World J. Gastroentero March 7; 13(9): 1384-1392 2007.
19. Maiti S., Misra J.C., “Peristaltic flow of fluid in a porous channel: a study having relevance to flow of bile within ducts in a pathological state”, arXIVII-10715797vI [math-ph] 8 july 2011.

20. Master, P. D. and Elman, R., “On the expulsion of bile by the gallbladder; and a reciprocal relationship with the sphincter activity”, The Journal of experimental medicine, Vol.44,173-198, 1926.
21. Mazer, N. A. and Carey, M. C., “Mathematical model of biliary lipid secretion: a quantitative analysis of physiological biochemical data from man and other species”, Journal of lipid research Vol. 25, 1984.
22. Navier-Stokes Equation: http://en.wikipedia.org/wiki/Navier%E2%80%93Stokes_equations.
23. Ooi, R.C., Luo, X. Y., Boonchin, S., Johnson, A. G. and Bird, N. C., “Fluid structure interaction (F.S.I) simulation of the human cystic duct”, Summer bioengineering conference 2003.
24. Ooi, R.C., Luo, X. Y., Chin, S., Johnson, A. G. and Bird, N. C., “The flow of bile in human cystic duct”, Journal of biomechanics 37(2004):1913-1922.
25. Pitt, H. A., Doty, J.E., Besten, D. and Kuchenbecker, S. L., “Stasis before gallstone formation: altered gallbladder compliance or cystic duct resistance”, Am J Surj., 143(1):144-9, 1982.
26. Rodkiewicz, C. M., and Otto, W. J., “On the Newtonian behavior of bile”, Journal of biomechanics Vol. 12.pp 609-612, 1978.
27. Rodkiewicz, C. M., Otto, W. J. and Scott, G. W., “Empirical relationship for the flow of bile”, Journal of biomechanics Vol. 12 pp. 411-413, 1979.
28. Suchi A., Models of biofluid flow in human biliary system, Thesis, DEI, 2013.
29. Yamada C., Tadataka K., Textbook of Gastroenterology (6 ed.). John Wiley & Sons 2011.